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**Resolving stem and progenitor cells in the adult mouse incisor through gene co-expression analysis.**

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**Public Summary:**

Investigations into stem cell-fueled renewal of an organ benefit from an inventory of cell type-specific markers and a deep understanding of the cellular diversity within stem cell niches. Using the adult mouse incisor as a model for a continuously renewing organ, we performed an unbiased analysis of gene co-expression relationships to identify modules of co-expressed genes that represent differentiated cells, transit-amplifying cells, and residents of stem cell niches. Through in vivo lineage tracing, we demonstrated the power of this approach by showing that co-expression module members *Lrig1* and *Igfbp5* define populations of incisor epithelial and mesenchymal stem cells. We further discovered that two adjacent mesenchymal tissues, the periodontium and dental pulp, are maintained by distinct pools of stem cells. These findings reveal novel mechanisms of incisor renewal and illustrate how gene co-expression analysis of intact biological systems can provide insights into the transcriptional basis of cellular identity.

**Scientific Abstract:**

Investigations into stem cell-fueled renewal of an organ benefit from an inventory of cell type-specific markers and a deep understanding of the cellular diversity within stem cell niches. Using the adult mouse incisor as a model for a continuously renewing organ, we performed an unbiased analysis of gene co-expression relationships to identify modules of co-expressed genes that represent differentiated cells, transit-amplifying cells, and residents of stem cell niches. Through in vivo lineage tracing, we demonstrated the power of this approach by showing that co-expression module members *Lrig1* and *Igfbp5* define populations of incisor epithelial and mesenchymal stem cells. We further discovered that two adjacent mesenchymal tissues, the periodontium and dental pulp, are maintained by distinct pools of stem cells. These findings reveal novel mechanisms of incisor renewal and illustrate how gene co-expression analysis of intact biological systems can provide insights into the transcriptional basis of cellular identity.

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